

84

**Notice of Allowability**

**Application No.**

09/982,968

**Examiner**

Jane Zara

**Applicant(s)**

GRISSOM ET AL.

**Art Unit**

1635

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 12-25-03.
2. ☒ The allowed claim(s) is/are 1-43.
3. ☒ The drawings filed on 22 October 2001 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of the:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).  
\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.  
(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached  
1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.  
(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.  
**Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |   |   |
|---|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)  | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)           |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                | 6. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date _____ |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),<br>Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment                   |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material          | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance  |
|   | 9. <input type="checkbox"/> Other _____   |

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jeffrey Ihnen on or about 3-22-04.

The application has been amended as follows:

Claim 1 (currently rewritten): A method of administering a bioactive agent to cells of a targeted tissue site of a subject which comprises administering to said subject an effective amount of the bioactive agent as a bioconjugate, wherein said bioconjugate comprises the bioactive agent and an organocobalt complex wherein the bioactive agent is covalently conjugated to the cobalt atom of the organocobalt complex through a non-reactive atom in the bioactive agent molecule, and wherein said bioconjugate is actively transported into said cells of said targeted tissue site and accumulates in an inactive form until activated by cleavage of the bioactive agent from the organocobalt complex, and which cells of a targeted tissue comprise receptors for the organocobalt complex that mediate endocytotic activity.

### **EXAMINER'S REASONS FOR ALLOWANCE**

The following is an examiner's statement of reasons for allowance: The claimed invention is free of the prior art of record because the prior art of record does not teach or fairly suggest a method of administering to target tissues a bioconjugate of a bioactive agent and an organocobalt complex wherein the bioactive agent is covalently conjugated to the cobalt atom through a non-reactive atom in the bioactive agent molecule, and which bioactive agent molecule is cleaved from the bioactive agent and is activated by cleavage from the organocobalt complex following cellular uptake and accumulation, and which target tissues and cells comprise organocobalt receptors that mediate endocytotic activity and cellular uptake of the organocobalt complex.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

### **EXAMINER'S COMMENTS**


Adequate representatives of bioactive agents, and non-reactive atoms therein, have been provided in the instant disclosure, including on pages 7-12, 52 and 64 of the specification. Adequate representatives of organocobalt complexes, including covalent attachment of bioactive molecules to the cobalt atom, have been provided throughout the instant specification, including on pages 12-14 and 35-38. The instant invention is enabled for administration to target tissues and cells comprising organocobalt receptors

because the instant disclosure and the prior art teach the administration of organocobalt compounds comprising vitamin B12 and cobalamin related compounds, including cyano-, hydroxo-, methyl- and adenosylcobalamin, to cells expressing the organocobalt receptors, and which target cells include rapidly proliferating cells (e.g. various neoplastic cells and tumors), bacteria, kidney and liver cells. The uptake of cobalamin related compounds has been manipulated in organisms using nitrous oxide and other pharmacologic agents including vitamin B12 and cobalamin compounds. Administration to target cells in an organism has been taught using intraperitoneal, intramuscular, intravenous and oral administration. Cleavage of bioactive agents from the organocomplex, and conversion from inactive to active agents have been taught throughout the instant specification, including pages 14, 43-47, 52-56, 61-62 and 65-68.

### ***Conclusion***

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



RAM R. SHUKLA, PH.D.  
PRIMARY EXAMINER

JZ  
~~3-13-04~~  
3/22/04